

November 27, 1956

Dear Dr. Calvin:

I was very much interested to see your article in the American Scientist recently; I have the journal of course, but if you can spare a reprint it would be a minor convenience.

I am enclosing a reprint which also stems from a talk at Amherst, about a year after yours, of which I was unaware. I fully agree that it is nonsense to think in terms of a unique event like the full-formed appearance of a "self-reproducing" protein or nucleic acid for elementary biopoiesis. For a time, I was searching for examples, like yours, on improvement of organic catalysis, even possibly with the hope of doing some model experimentation. But my genetic training has been catching up with me, and I now think we have to grope ~~with uncertainty~~ for another principle as well, what von Neumann succinctly called the "screws" that hold the S.R. complexes together, —what might be considered the linear scaffolding on which the elementary genes are assembled. The point is that so long as one "elementary autocatalytic unit" succeeds another one, there is no scope for evolving the kind of complexity that we need for plausible rates of mutation, selection etc. You would have  
and a limited numbers of bits of information  
secured at each stage.

$A \rightarrow A' \rightarrow A'' \rightarrow A'''$

But if there were some way of stringing the bits together, so that

$A-A$ ,  $A-A'$ ,  $A'-A'$  etc would each (tend to) "replicate themselves" (i.e., encourage the preferential synthesis of their own type) you would have a pathway for building unlimited complexity. Now a series of sucrose-crystals on a string will replicate the same sequence of crystal-faces in a saturated sugar solution; "all we need" is a way to slice the "new growth" and to replicate the string. I am still hopeful we may be able to find some relatively simple inorganic systems that will meet these specifications.

However, there is not much time left to do these naive experiments. The replication of DNA, along the lines of the ideas impelled by Watson and Crick seems to <sup>leave</sup> only a matter of time for a full in vitro reconstruction, in which case this will be the first and perhaps final "model". But there may still be some point in looking for simpler and perhaps cosmically more likely starting points. I would <sup>be</sup> interested to hear if you have any concrete suggestions: I wonder myself if the silicates don't offer the most promise.

Yours sincerely,

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Professor of Genetics